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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	**PAPER NUMBER**
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,685	BENOWITZ, LARRY I.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/05; 07/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

The abstract of the disclosure is objected to because the first page of the WIPO document filed 3/21/2005, which has an abstract, has also been used as the abstract sheet in the instant specification. This is not acceptable if the instant claims are determined to be allowable at a later stage. The Office requires the abstract to be typed on a separate sheet of paper even though applicants intend using the abstract on the WIPO document for the instant application. Hence, applicants are requested to kindly type the abstract appearing on the first page of the WIPO document (WO 2004/028468) on a separate sheet and file the same.

Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the regeneration of axons on retinal ganglion cells by administration of mannose and forskolin and a composition comprising mannose and a pharmaceutically acceptable carrier, does not reasonably provide enablement for the treatment of any neurological disorder as broadly claimed in instant claim1 and all the disorders recited in claims 10-11, 18-22 and composition claims 23-26. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The state of the prior art
(C) The level of predictability in the art
(D) The amount of direction provided by the inventor
(E) The existence of working examples
(F) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claim 1 is drawn to a method of treating a neurological disorder by administering a therapeutically effective amount of a hexose. The breadth of the claims is seen to include several disorders and conditions including ones that are not known at the time of filing of the instant application. The recitation, a hexose is also seen to include any hexose. Instant claim 10 also recites several diseases/disorders. The term injury is broad and is seen to include any type of injury. Claim 22 also recites the broad terms neurological disorder.

The state of the prior art

The examiner notes that the art cited by the applicants and the prior art of record, Thanos et al (Investigative ophthalmology and Visual Science, 2000, 41(12), 3943-54) is drawn to axonal regeneration. However, there is no teaching of the treatment of other neurological

diseases and conditions in the prior art. One of ordinary skill in the art would not extrapolate the information in the prior art to the treatment of all of the said diseases and conditions.

The level of predictability in the art

The broad term, neurological diseases and the other diseases recited in instant claims 1 and 10 all have different etiologies. For example Huntington's disease is due to degeneration of small cell population and decrease in levels of γ-aminobutyric acid (Merck Manual 16th Edn, 1992, pages 1493-94). Alzheimer's type dementia is due to plaques and neurofibliatory tangles in the brain (The Merck Manual, 16th Edn. 1992, pages 1403-04). The cause of Multiple Sclerosis, a CNS disease is unknown (The Merck Manual, 16th Edn. 1992, pages 1488-89). With different etiologies for several and unknown causes for some diseases it is highly unpredictable that administration of a hexose like mannose or gulose or glucose-6-phosphate either alone or in combination with a cAMP modulator like oncomodulin or TGF-β can treat any and all of the disorders as instantly claimed.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the treatment of all the neurological disorders as instantly claimed. The specification also fails to direct the skilled artisan in correlative prior art procedures which might provide the basis for the said treatment.

The existence of working examples

The working examples set forth in the instant specification are drawn to the effect of mannose and mannose forskolin combination on rat ganglion cells. The results just show the

growth of axons regeneration. Despite these examples there is little enabling disclosure for the treatment of all of the neurological disorders as instantly claimed. Applicant has given working examples of the effect of the compounds on rat ganglion cells only. Based on this one of ordinary skill in the art cannot predict or extrapolate it to the treatment of all the diseases and conditions as instantly claimed. The growth of axons alone cannot treat all of the disorders as instantly claimed.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the use of the instant compounds for the treatment of neurological diseases as instantly claimed. One of ordinary skill in the art would have to carry out experimentation with several different disorder models in order to determine the efficacy of the said compounds in the said methods of treatment.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-7 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites membrane depolarization as one of the Markush members for cAMP modulator. All the other members recited are compounds. The terms, "membrane depolarization"

does not refer to a compound or a molecule but refers to an effect produced. It is not clear what applicants intend.

Claim 5 recites, "a macrophage derived factor". The metes and bounds of the said recitation are not clear and render the claim indefinite.

Claim 26 is drawn to the composition of claim 25 further comprising oncomodulin. According to the applicant's oncomodulin, a macrophage-derived factor is a cAMP modulator (see instant claim 6). Does applicant intend a composition comprising D-mannose, oncomodulin and another cAMP modulator or does the applicant mean, "wherein the cAMP modulator is oncomodulin" in claim 26.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 31-32 and 34-37 of copending Application No. 10/580364 ('364). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Instant Claim 1 is drawn to a method of treatment of neurological disorders comprising administration of an effective amount of a hexose. Dependent claims 2-21 recite limitations drawn to the type of hexose and other active agents and specific disorders.

Claim 31 of '364 is drawn to a method treating a neurological disorder comprising administering an NgR antagonist and an agent that activates the growth of CNS neurons. Dependent claims 32 and 34-37 recites specific disorders and oncomodulin, growth factors and hexoses as the active agents.

Claims 31-32 and 34-37 of '364 differ from the instant claims in that the instant claims do not employ an NgR antagonist. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the active agents as recited in the instant claims could be successfully employed in the method of '364 too since both are used for the treatment of neurological disorders.

In determining the differences between the prior art and the claims, the question is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references

themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). In the instant case, '364 teaches the use of some of the active agents applicant claims. Although the claims of '364 employ an NgR antagonist in combination with the active agents instantly claimed, one of ordinary skill in the art would readily recognize that the scheme taught by '442 could be employed in the instant method. One of ordinary skill in the art is seen as one having an M.D./PhD. The use of known members of classes of agents in a method to effectuate the same type of treatment taught in the prior art is not seen to render the instantly claimed method unobvious over the art. Once the general method of using the active agents has been shown to be old, the burden is on the applicant to present reason or authority for believing that the starting compound (s) would alter the nature of the product or the operability of the method and thus the unobviousness of the method of treatment.

Claims 22-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18-20 and 22 of copending Application No. 11/804,295 ('295). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Instant Claim 22 is drawn to a kit comprising D-mannose as a pharmaceutical agent together with a pharmaceutical carrier. Dependent claim 23 and 24 are drawn to further comprising a cAMP modulator and oncomodulin as the modulator. Instant claim 24 is drawn to

a formulation comprising D-mannose and cAMP modulator. Dependent claim 26 is drawn to the formulation wherein the modulator is oncomodulin.

Claims 18-20 of '295 is drawn to a composition comprising oncomodulin, a cAMP modulator and dependent claim 22 is drawn to the composition further comprising mannose.

Claim 22 of '295 differs from the instant claims in that the instant claims do not recite any sugar other than mannose. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the active agents as recited in the instant claims could be successfully employed in the method of '295 too.

In determining the differences between the prior art and the claims, the question is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). In the instant case, '295 teaches the use of some of the active agents applicant claims. Although the claims of '295 recites that mannose derivatives and inosine can be used in addition to mannose, one of ordinary skill in the art would readily recognize that the combination of oncomodulin and mannose, as taught by '295 could be employed to make the composition as instantly claimed. One of ordinary skill in the art is seen as one having an M.D./PhD. The use

of known members of classes of agents in a method to make the same type of composition taught in the prior art is not seen to render the instantly claimed composition unobvious over the art. Once the general method of using the active agents has been shown to be old, the burden is on the applicant to present reason or authority for believing that the starting compound (s) would alter the nature of the product or the operability of the composition comprising the same.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-6, 10, 15-17 and 21-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 7-10 and 12-13 of U.S. Patent No. 6,855,690 ('690). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Instant Claim 1 is drawn to a method of treatment of neurological disorders in a human comprising administration of an effective amount of a hexose. Dependent claims 2-6, 10, 15-17 and 21-22 recite limitations drawn to the type of hexose including mannose and other active agents and specific disorders, which includes retina or optic nerve damage, optic nerve damage due to glaucoma and retina damage due to macular degeneration.

Claim 1 of '690 is drawn to a method treating optic nerve or retina damage in a human comprising administering a composition comprising oncomodulin. Dependent claims 2-4, 7-10 and 12-13 recite cAMP modulators including oncomodulin, growth factors and mannose or mannose derivatives as the active agents.

Claims 1-4, 7-10 and 12-13 of '690 differ from the instant claims in that the instant claims do not employ a mannose derivative. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the active agents as recited in the instant claims could be successfully employed in the method of '690 too since both are used for the treatment of neurological disorders. One of skill in the art also knows that derivatives of active agents are also routinely used in making compositions and in methods of treatment.

In determining the differences between the prior art and the claims, the question is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). In the instant case, '690 teaches the use of the some of the active agents applicant claims. Although the claims of '364 employ a mannose derivative in addition to mannose, one of ordinary skill in the art would readily recognize that the composition taught by '690 could be employed in the instant method. One of ordinary skill in the art is seen as one having an M.D./PhD. The use of known members of classes of agents in a method to effectuate the same type of treatment taught in the prior art is not seen to render the instantly claimed method unobvious over the art. Once the general method of using the active agents has been shown to be

old, the burden is on the applicant to present reason or authority for believing that the starting compound (s) would alter the nature of the product or the operability of the method and thus the unobviousness of the method of treatment.

Claims 22-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 7,238,529 ('529). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Instant Claim 22 is drawn to a kit comprising D-mannose as a pharmaceutical agent together with a pharmaceutical carrier. Dependent claim 23 and 24 are drawn to further comprising a cAMP modulator and oncomodulin as the modulator. Instant claim 24 is drawn to a formulation comprising D-mannose and cAMP modulator. Dependent claim 26 is drawn to the formulation wherein the modulator is oncomodulin.

Claims 1-2 of '529 are drawn to a kit comprising a combination of oncomodulin, a cAMP modulator and axogenic factor, wherein the axogenic factor can be mannose, a mannose derivative or inosine.

Claims 1-2 differ from the instant claims in that the instant claims do not recite any sugar other than mannose. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the active agents as recited in the instant claims could be successfully employed in the kit of '529 too. In determining the differences between the prior art and the claims, the question is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Obviousness can only

be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). In the instant case, '529 teaches the use of some of the active agents applicant claims. Although the claims of '529 recites that mannose derivatives and inosine can be used in addition to mannose, one of ordinary skill in the art would readily recognize that the combination of oncomodulin and mannose, as taught by '529 could be employed to make the kit and composition as instantly claimed. One of ordinary skill in the art is seen as one having an M.D./PhD. The use of known members of classes of agents in a method to make the same type of composition taught in the prior art is not seen to render the instantly claimed composition unobvious over the art. Once the general method of using the active agents has been shown to be old, the burden is on the applicant to present reason or authority for believing that the starting compound (s) would alter the nature of the product or the operability of the composition comprising the same.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Sherman et al (US 4,471,114).

Sherman teaches an effluent which comprises a aqueous solution of D-mannose. This reads on instant claim 25, which is drawn to a pharmaceutical agent (D-mannose) together with a pharmaceutically acceptable carrier (water). See col. 1, Example 4. According to Figure 4 the effluent concentration has about 1.5% of mannose. This is seen as an effective dose. Even though Sherman does not teach the composition in a packaging material as instantly claimed, it is well within the skill level of the artisan to package such a composition with a label.

Conclusion

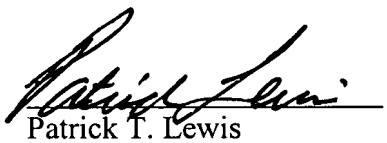
Claims 1-26 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK



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